AMENDMENT TO THE SPECIFICATION

On page 12, please replace the paragraph beginning, "**Figure 20**: Schematic illustration of RSV-lacZ..." with the following paragraph:

--**Figure 20**: Schematic illustration of RSV-lacZ constructs (SEQ ID NOs:6-8, 91 & 92).--

On page 83, please replace the paragraph beginning, "Two phosphorylation mutations containing two serine site substitutions..." with the following paragraph:

--Two phosphorylation mutations containing two serine site substitutions (SSSAA [PP2]) (SEQ ID NO:88) or five serine site substitutions (LRLAA [PP5]) (SEQ ID NO:89) were introduced into rA2. Mutations were initially introduced into the P protein gene in an RSV cDNA subclone, pRSV-(A/S), which contains the RSV A2 sequences from nucleotide (nt 2128 (AvrII) to (nt 4485 (SacI), by the QuikChange Site-Directed Mutagenesis kit (Stratagene). The AvrII-SacI fragment carrying the introduced mutations was then inserted into the full-length RSV A2 antigenomic cDNA clone, pRSVC4G. pRSVC4G contains the C-to-G change at the fourth position of the leader region in the antigenomic sense. Two recombinant viruses were recovered from the transfected HEp-2 cells and designated as rA2-PP2 (SSSAA) (SEQ ID NO:88) and rA2-PP5 (LRLAA) (SEQ ID NO:89). The recovered viruses were plaque purified and amplified in Vero cells. Virus titer was determined by plaque assay on Vero cells, and the plaques were enumerated after immunostaining with a polyclonal anti-RSV A2 serum (Biogenesis). The presence of each mutation in the recombinant viruses was confirmed by sequence analysis of the P protein gene cDNA amplified by reverse transcription-PCR (RT-PCR) with viral genomic RNA as template.--

On page 86, please replace the paragraph beginning, "The five phosphorylation sites in P protein at serines 116, 117, and 119..." with the following paragraph:

--The five phosphorylation sites in P protein at serines 116, 117, and 119 (116/117/119 [central region]) and 232 and 237 (232/237 [C terminal region]) are well conserved in the pneumoviruses. To examine the role of P protein phosphorylation in virus

replication, the serine residues in these two clusters were mutagenized to remove their phosphorylation potential. The three serines in the central region were substituted for with leucine, arginine, and leucine, respectively (Mutl [LRLSS])]) (SEQ ID NO:85), or aspartic acid to mimic the negative charges of the phosphate groups (Mut2 [DDDSS])]) (SEQ ID NO:86). The two serines in the C-terminal region were changed to either aspartic acid (Mut3 [SSSDD])]) (SEQ ID NO:87) or alanine (Mut4 [SSSAA])]) (SEQ ID NO:88). In addition, all five serines were changed to LRLAA (Mut5)]) (SEQ ID NO:89) or LRLDD (Mut6)]) (SEQ ID NO:90) to eliminate all of the major P protein phosphorylation sites. The positions of the substituted residues in each mutant are summarized in **Figure 14**.--

On page 86, please replace the paragraph beginning, "The functions of the altered P protein were evaluated in the RSV CAT minigenome..." with the following paragraph:

--The functions of the altered P protein were evaluated in the RSV CAT minigenome assay. MVA-T7-infected HEp-2 cells were transfected with pRSVCAT along with pL, pN, and wild-type or mutant pP, and expression of the CAT gene was measured by CAT-ELISA. The function of each P protein mutant was calculated as its relative activity compared to that of wild-type P protein. Error bars represent the standard deviation of three replicate experiments. As shown in **Figure 15A**, substitution of the three central serines by LRL (lane 2) had little effect on protein function, but substitution of these three residues by aspartic acid (DDD, lane 3) almost completely abolished the protein's function. To evaluate each position independently, three single aspartic acid substitutions were made. As shown in **Figure 15A**, S116D was not functional (lane 4), and the other two mutants (SI17D, lane 5; S119D, lane 6) remained functional, albeit at a reduced level. However, substitution of Ser-116 or Ser-117/119 by alanine had no effect on P protein function in the minigenome assay. These observations indicated that the serines at 116/117/119 were not required for P protein function and that the aspartic acid residues might have a structural impact on the P protein. P protein mutation at the C-terminal phosphorylation sites, 232/ 237, substituted for by alanine (lane 9) or aspartic acid (lane 10), reduced the P protein function by approximately 10 to 20% (**Figure 15A**). A slightly reduced level of reporter gene activity was detected in cells expressing mutant P protein that had all five serines removed (LRLAA, lane 11 (SEQ ID NO:89); LRLDD, lane 12 (SEQ ID NO:90)). All of the P protein mutants expressed a level of P protein comparable to that of the wild-type in these assays as determined by Western

blotting. Therefore, the minigenome assay indicated that removal of all five phosphorylation sites from RSV P protein did not have a significant impact on protein function in vitro. The difference in the protein activity among these P protein mutants could be due to the reduction of P protein phosphorylation or due to an alteration of P protein structure caused by substitutions of the phosphorylation sites.--

On page 87, please replace the paragraph beginning, "Since Mut3 (DDDSS) almost completely abolished the P protein..." with the following paragraph:

--Since Mut3 (DDDSS) (SEQ ID NO:86) almost completely abolished the P protein function, it was thus interesting to know if this mutant would exhibit any dominant-negative effect on the function of wild-type P protein. Plasmid pP-DDD was cotransfected with the wild-type P protein plasmid pP-wt in different ratios together with 0.4 μg of pN and 0.2 μg of pL to determine if this mutant would interfere with wild-type P protein function in the minigenome assay (**Figure 15B**). The T7 expression vector (pCITE) was used as a control. The levels of reporter gene expression (expressed as a percentage of that of wild-type P protein) decreased in correlation with the decreased amount of wild-type pP, which was most likely due to suboptimal ratio among the N, P, and L proteins. However, pP-DDD reduced the reporter gene expression at a level similar to that of the pCITE vector control. Thus, it appeared Mut3 did not have any dominant-negative effect on wild-type P protein function.—

On page 88, please replace the paragraph beginning, "To examine the effect of P protein phosphorylation mutations on virus replication..." with the following paragraph:

--To examine the effect of P protein phosphorylation mutations on virus replication, two mutants were introduced into the RSV A2 antigenomic cDNA clone: one with mutations at the two C-terminal serines (SSSAA [PP2]) (SEQ ID NO:88) and the other with mutations at five serines (LRLAA [PP5]) (SEQ ID NO:89). Both recombinant viruses were obtained from the transfected cDNA and designated rA2-PP2 and rA2-PP5, respectively. Each virus was amplified in Vero cells, and both the released and cell-associated viruses were collected. rA2-PP2 and rA2-PP5 had titers of approximately 2 x 10^7 PFU/ml in Vero cells, a level comparable to that of wild-type rA2.--